

Increased Citrulline Amino Aciduria/Urea Cycle Disorder

Differential Diagnosis: Citrullinemia I, argininosuccinic acidemia; citrullinemia II (citrin deficiency), pyruvate carboxylase deficiency.

Condition Description: The urea cycle is the enzyme cycle whereby ammonia is converted to urea. In citrullinemia and in argininosuccinic acidemia, defects in ASA synthetase and lyase, respectively, in the urea cycle result in hyperammonemia and elevated citrulline.

Medical Emergency: Take the Following IMMEDIATE Actions

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Immediately consult with pediatric metabolic specialist. (See attached list.)
- Evaluate the newborn (poor feeding, vomiting, lethargy, hypotonia, tachypnea, seizures and signs of liver disease). Measure blood ammonia.
- If any sign is present or infant is ill, initiate emergency treatment for hyperammonemia in consultation with metabolic specialist.
- Transport to hospital for further treatment in consultation with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing and management, as recommended by specialist.
- Initial testing: Immediate plasma ammonia, plasma quantitative amino acids.
- Repeat newborn screen if second screen has not been done.
- Provide family with basic information about hyperammonemia.
- Report findings to newborn screening program.

Diagnostic Evaluation: Plasma ammonia to determine presence of hyperammonemia. In citrullinemia, plasma amino acid analysis will show increased citrulline, whereas in argininosuccinic acidemia, argininosuccinic acid will also be present. Orotic acid may be increased in both disorders, which can be determined by urine organic acid analysis. In citrin deficiency, liver enzymes, lactic acid and bilirubin may be elevated. For pyruvate carboxylase deficiency, blood lactate and pyruvate will be elevated.

Clinical Considerations: Citrullinemia and argininosuccinic acidemia can present acutely in the newborn period with hyperammonemia, seizures, failure to thrive, lethargy, and coma. Later signs include mental retardation. Citrin deficiency may present with cholestatic liver disease in the newborn period. Pyruvate carboxylase deficiency produces coma seizures and life-threatening ketoacidosis. Treatment for ASA and citrullinemia is to promote normal growth and development and to prevent hyperammonemia.

Additional Information:

Gene Tests/Gene Clinics

<http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=HWrt-uSqLup&gry=&fcn=y&fw=b8Mv&filename=/profiles/ctlm/index.html>

Genetics Home Reference

<http://ghr.nlm.nih.gov/condition=citrullinemia>

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<http://www.newbornscreening.info/Pro/aminoaciddisorders/ASAS.html>
<http://www.newbornscreening.info/Parents/aminoaciddisorders/ASAS.html>
<http://www.newbornscreening.info/Parents/aminoaciddisorders/ASAL.html>
<http://www.newbornscreening.info/Pro/aminoaciddisorders/ASAL.html>

Newborn Screening FACT Sheet

Citrullinemia (CIT)

What is CIT?

CIT is a type of amino acid disorder. People with CIT can't rid the body of ammonia. It is made when the body breaks down protein and amino acids.

What Causes CIT?

Enzymes help start chemical reactions in the body. CIT is a condition called "urea cycle disorder." It happens when an enzyme called "argininosuccinic acid synthetase" (ASAS) is either missing or doesn't work right. ASAS helps break down amino acids. It also removes ammonia from the body. The amino acid citrulline builds up in the blood when ASAS doesn't work. Ammonia also builds up. Too much ammonia can cause brain damage. It can cause death if untreated.

What Symptoms or Problems Occur with CIT?

[Symptoms are something out of the ordinary that a parent notices.]

Some of the first symptoms of high ammonia are:

- poor appetite
- too much sleepiness or lack of energy
- irritable mood
- vomiting

If untreated, high ammonia can cause:

- muscle weakness
- breathing problems
- problems staying warm
- seizures
- swelling of the brain
- coma, sometimes leading to death

What is the Treatment for CIT?

1. Low-protein diet and/or special medical foods and formula – The best treatment for CIT is a very low-protein diet (avoid meat, fish, eggs, milk products, nuts and beans). There are medical foods such as special low-protein flours, noodles, and rice available. A dietitian will make a food plan for your child. Dietitians know what are the right foods to eat. The doctor or dietitian may give your baby a special formula with the right nutrients and amino acids. People with CIT should follow their food plan for life.

2. Medication – Medications can also rid the body of ammonia. Children with CIT take these by mouth or feeding tube.

3. Blood tests – Regular blood tests will check your child's amino acid and ammonia levels.

Things to Remember

Call your doctor right away if your child has any of the following:

- loss of appetite
- low energy or too much sleepiness
- vomiting
- fever
- infection or illness
- behavior or personality changes (such as crying for no reason)
- problems walking or balancing
- bad headache

Children with high ammonia often need to be treated in the hospital.

Argininosuccinic Acidemia (ASA)

What is ASA?

ASA is a type of amino acid disorder. People with this condition can't remove ammonia from the body. Ammonia is a harmful substance. It is made when the body breaks down protein and amino acids for use by the body.

What Causes ASA?

ASA is a "urea cycle disorder" (UCD). ASA happens when an enzyme called "argininosuccinic acid lyase" (ASAL) is missing or not working. Enzymes help start chemical reactions in the body. Ammonia builds up in the blood when there is a problem with the ASAL enzyme. Too much ammonia in the blood can cause brain damage. It can also cause death if not treated.

What Symptoms or Problems Occur with ASA?

[Symptoms are something out of the ordinary that a parent notices.]

There are two kinds of ASA. The severe form starts in babies. They are healthy when born, but soon show symptoms of high ammonia levels. The milder form of ASA starts in childhood.

Some of the first symptoms of high ammonia are:

- poor appetite
- too much sleepiness or no energy
- irritable mood
- vomiting

If not treated, high ammonia can cause:

- muscle weakness
- breathing problems
- problems staying warm
- seizures
- swelling of the brain
- coma, sometimes leading to death

The milder form can also cause mental retardation, seizures, a large liver, and skin and hair problems.

What Is the Treatment for ASA?

The following treatments are often used for babies and children with ASA:

1. Low-protein diet and/or special

medical foods and formula – The best treatment is a very low-protein diet. There are medical foods such as special low-protein flours, noodles, and rice available. A dietitian will make a food plan for your child.

Dietitians know what are the right foods to eat. Your child will need to eat a low-protein diet for life. The doctor or dietitian may give your baby a special formula that has the right nutrients and amino acids.

2. Medication – The doctor might prescribe arginine supplements for your child. Other medicines may be used to prevent high ammonia.

3. Blood tests – Regular blood tests will check your child's amino acid and ammonia levels.

Things to Remember

Children with high ammonia often need to be treated in the hospital. Call your doctor right away if your child has any of the following:

- loss of appetite
- low energy or too much sleepiness
- vomiting
- fever
- bad headache
- infection or illness
- behavior or personality changes (such as crying for no reason)
- problems walking or balancing

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